(19) World Intellectual Property Organization

International Bureau





(43) International Publication Date 13 October 2005 (13.10.2005)

PCT

(10) International Publication Number WO 2005/094863 A1

(51) International Patent Classification⁷: A 39/00, G01N 33/53, A61P 35/00

A61K 38/00,

(21) International Application Number:

PCT/DK2005/000218

(22) International Filing Date: 30 March 2005 (30.03.2005)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

PA 2004 00506 60/558,123

30 March 2004 (30.03.2004) DK 1 April 2004 (01.04.2004) US

(71) Applicant (for all designated States except US): DEN KGL.VETERINÆR-OG LANDBOHØJSKOLE [DK/DK]; Bülowsvej 17, DK-1870 Frederiksberg C (DK).

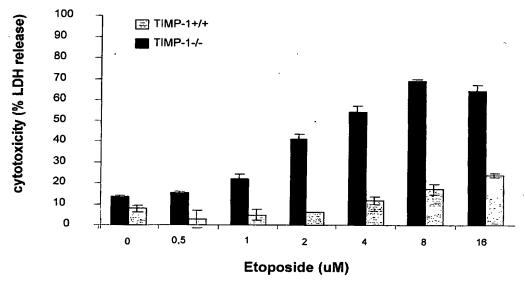
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): RØMER, Maria

Unni [DK/DK]; Ved Volden 10, 5.th., DK-1425 Copenhagen K (DK). LADEMANN, Ulrik Axel [DK/DK]; Gladsaxvej 34, 2.tv., DK-2860 Søborg (DK). HOFLAND, Kenneth Francis [DK/DK]; Koldinggade 20, 4.th., DK-2100 Copenhagen Ø (DK). JENSEN, Peter Buhl [DK/DK]; Maglehøj 100, DK-3520 Farum (DK). VAN GELDER, Marion Ellen Meijer [NL/NL]; Jan Tooropstraat 65, NL-3262 TG Oud-Beijerland (NL). FOEKENS, Johannes Albert [NL/NL]; Filosofentuin 35, NL-2908 XA Capelle aan den Ijssel (NL). RASMUSSEN, Anne-Sofie Schrohl [DK/DK]; Hindegade 8,3.tv., DK-1303 Copenhagen K (DK). BRÜNNER, Nils Age [DK/DK]; Tranevænget 8,3.tv., DK-2900 Hellerup (DK). USHER, Pernille Autzen [DK/DK]; Trepkasgade 4, 4.th., DK-2100 Copenhagen Ø (DK).

- (74) Agent: INSPICOS A/S; Bøge Allé 3, DK-2970 Hørsholm (DK).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,

[Continued on next page]

(54) Title: IMPROVEMENTS IN CANCER TREATMENT AND CANCER TREATMENT EFFICACY PREDICTION BY BLOCKING AND DECTING PROTEASE INHIBITORS



(57) Abstract: Disclosed is a method for improving cancer therapy that relies on induction of apoptosis in malignant cells. It has been found that docking of protease inhibitors PAI-1 and TIMP-1 renders malignant cells expressing these inhibitors more sensitive to apoptosis, whereas non-malignant cells do not change their sensitivity to apoptosis induction. It is therefore possible to increase the effect of various anti-cancer treatments in a rational manner and to predict whether or not an apoptosis-inducing cancer treatment will be effective in a patient or not. The invention also provides for methods of identifying agents that inhibit the apoptosis sensitivity modulating effects of protease inhibitors and to methods of identifying anti-cancer compounds that are not dependent on an apoptosis inducing mechanism which can be modulated by protease inhibitors.

WO 2005/094863 A1

KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,

SE. SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.